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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,423	09/19/2003	Blas Frangione	05986/100K433-US2	8605

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EXAMINER	
GAMETT, DANIEL C	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/666,423	FRANGIONE ET AL.	
	Examiner	Art Unit	
	Daniel C. Gamett, PhD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-15,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/19/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of 10-15, 21, and 22, drawn to an isolated peptide comprising the amino acid sequence of SEQ ID NO:1 and a method for inducing an immune response comprising administering said peptide, in the reply filed on 02/24/2006 is acknowledged.

2. Claims 1-9 and 16-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 02/24/2006.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 10-15, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6866849 ('849), issued March 15, 2005, with priority to November 30, 1998, in view of Ghanta *et al.*, 1996, J. Biol. Chem. 271(47):29525-29528, US Patent 6962707 ('707), issued November 8, 2005, with priority to November 30, 1998, and Maillere *et al.*, 1995, Molecular Immunology 32(17/18): 1377-1385. Claims 10-15 are drawn to an isolated peptide comprising the amino acid sequence of SEQ ID NO:1, which consists of the N-terminal 30 amino acids of human amyloid β (Aβ), with optional modifications comprising 4-10 lysine or aspartate residues at either end or (in

claims 13 and 14) amidation of the C-terminus. Claims 21 and 22 are drawn to a method for inducing an immune response comprising administering said peptide. The '849 patent teaches (throughout) administration of a peptide consisting of the first 39 amino acids (thus comprising amino acids 1-30) of Aβ for the purpose of evoking a therapeutic antibody response (see claim 36). The '849 patent does not, however, teach the modifications recited in the instant claims. Ghanta *et al.*, citing earlier work, teach that the unmodified amino terminal peptide of Aβ to forms neurotoxic aggregates and further teach that toxicity is inhibited in Aβ aggregates that incorporate Aβ peptides that are covalently modified by addition of an element that disrupts β-sheet formation (see abstract). Ghanta *et al.*, further identify lysine hexamers as effective disrupting elements (p. 29525, 1st paragraph under "Experimental Procedures" and figures 1, 3-5). One of skill in the art would recognize that the ability of the unmodified amino terminal peptide of Aβ to form neurotoxic aggregates cited by Ghanta *et al.*, would work against the therapeutic benefit of antibodies evoked by use of the unmodified amino terminal peptide of Aβ as an immunogen as taught by the '849 patent. Therefore, it would have been obvious for one of skill in the art at the time the invention was made to combine the teachings of the'849 patent, which provide for a therapeutically beneficial immune response, with the teachings of Ghanta *et al.*, which provide a means to reduce the toxicity of the immunogen, with a reasonable expectation of success. The skilled artisan would expect that the net benefit of the combined methods would be greater than that taught in the '849 patent. Further expectation of success is provided by the '707 patent, which teaches a therapeutic agent comprising polylysine or polyglutamic acid linked to the amino or carboxyl terminus of an immunogenic, natural Aβ peptide (see claim 11).

The '707 patent does not teach polyaspartate or the 4-10 amino acid limit, but this teaching does indicate that addition of polyamino acids to an Aβ peptide immunogen is potentially beneficial and at least feasible. The substitution of aspartate for glutamate is conservative, as both are acidic amino acids. Ghanta *et al.*, provide the rationale for the use of six (within the range of 4-10) amino acids as noted above.

5. None of the aforementioned references teach amidation of the C-terminus of the peptide to be administered, as required in claims 13 and 14. Maillere *et al.*, teach that C-terminal amidation decreases proteolytic degradation of peptides and enhances the capacity of the peptide to activate lymphocytes (see abstract). Therefore this modification would be obvious to a skilled artisan contemplating in vivo administration of a peptide for any purpose, especially for evoking an immune response.

Conclusion

6. No claims are allowed.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. WO 99/27944 published 10 June 1999 (IDS) teaches therapeutic administration of a peptide consisting of the first 39 amino acids page 14, lines 25-28, for example.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D.,whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
17 May 2006